

WHAT IS CLAIMED IS:

1. A method for preparing a nucleic acid sample for hybridization to a nucleic acid array, said method comprising:

providing a nucleic acid sample, said nucleic acid sample comprising mRNA;

amplifying the mRNA to produce cRNA; and

fragmenting the cRNA with an RNase enzyme to provide fragments.

2. The method of claim 1 further comprising the step of hybridizing said fragments to an oligonucleotide probe array.

3. The method of claim 1 wherein said RNase enzyme is selected from the group consisting of Ribonuclease III, Nuclease S1, RNase A, RNase H, RNase T1, and Mung Bean nuclease.

4. The method of claim 3 wherein said RNase enzyme is Ribonuclease III.

5. The method of claim 1 wherein said fragments have an average size of between about 20 to 500 nucleotides.

6. The method of claim 5 wherein said fragments have an average size of between about 25 to 200 nucleotides.

7. The method of claim 6 wherein said fragments have an average size of between about 50 to 100 nucleotides.

8. A method for detecting hybridization of a nucleic acid sample to a nucleic acid array, said method comprising:

providing a nucleic acid sample comprising mRNA transcripts of one or more genes;

reverse transcribing said nucleic acid sample with a reverse transcriptase and a promoter consisting of oligo dT and a sequence encoding the phage T7 promoter to provide single stranded DNA template;

synthesizing double stranded cDNA from said single stranded DNA template using DNA polymerase to provide cDNA template;

transcribing said cDNA template with T7 RNA polymerase to provide cRNA;

fragmenting said cRNA with an RNase to provide fragmented cRNA; and

hybridizing said fragmented cRNA to a nucleic acid array.

9. The method of claim 8 wherein said nucleic acid array is an oligonucleotide probe array attached to a support.

10. The method of claim 9 wherein said oligonucleotide probe array has at least about 100 probes per square centimeter.

11. The method of claim 8 wherein said RNase enzyme is selected from the group consisting of Ribonuclease III, Nuclease S1, RNase A, RNase H, RNase T1, and Mung Bean nuclease.

12. The method of claim 11 wherein said RNase enzyme is Ribonuclease III.

13. The method of claim 8 wherein said fragments have an average size of between about 20 to 500 nucleotides.

14. The method of claim 13 wherein said fragments have an average size of between about 25 to 200 nucleotides.

15. The method of claim 14 wherein said fragments have an average size of between about 50 to 100 nucleotides.

16. A method for preparing cRNA for hybridization to an oligonucleotide probe array, said method comprising:

providing cRNA;

fragmenting said cRNA with an RNase enzyme to provide fragmented cRNA.

17. The method of claim 16 wherein said RNase enzyme is selected from the group consisting of Ribonuclease III, Nuclease S1, RNase A, RNase H, RNase T1, and Mung Bean nuclease.

18. The method of claim 17 wherein said RNase enzyme is Ribonuclease III.

19. The method of claim 16 wherein said fragments have an average size of between about 20 to 500 nucleotides.

20. The method of claim 19 wherein said fragments have an average size of between about 25 to 200 nucleotides.

21. The method of claim 20 wherein said fragments have an average size of between about 50 to 100 nucleotides.

22. The method of claim 16 wherein said cRNA is labeled with biotin.

23. The method of claim 16 further comprising the step of end labeling said fragmented cRNA.

24. The method of claim 23 wherein said end labeling is with biotin.

25. A method for labeling an RNA sample comprising

providing an RNA sample;

fragmenting said RNA sample with an RNase enzyme to produce RNA fragments; and end-labeling said RNA fragments with a detectable label.

26. A method according to claim 25 wherein said RNA sample is selected from the group consisting of total RNA, mRNA and cRNA.
27. The method of claim 25 wherein said RNase enzyme is selected from the group consisting of Ribonuclease III, Nuclease S1, RNase A, RNase H, RNase T1, and Mung Bean nuclease.
28. The method of claim 27 wherein said RNase enzyme is Ribonuclease III.
29. The method of claim 25 wherein said fragments have an average size of between about 20 to 500 nucleotides.
30. The method of claim 29 wherein said fragments have an average size of between about 25 to 200 nucleotides.
31. The method of claim 30 wherein said fragments have an average size of between about 50 to 100 nucleotides.
32. The method of claim 25 wherein said detectable label is biotin.
33. The method according to claim 25 wherein said step of end labeling is performed with T4 RNA ligase.
34. A method for detecting the presence an RNA molecule in an RNA sample, said method comprising
- providing an RNA sample;
- fragmenting said cRNA with an RNase enzyme to provide RNA fragments;
- end-labeling said RNA fragments with a detectable label to provide end-labeled RNA fragments; and
- hybridizing said end-labeled RNA fragments to a nucleic acid array.

35. A method according to claim 34 wherein said nucleic acid array is an oligonucleotide array.
36. A method according to claim 34 wherein said RNA sample is selected from the group consisting of total RNA, mRNA and cRNA.
37. The method of claim 34 wherein said RNase enzyme is selected from the group consisting of Ribonuclease III, Nuclease S1, RNase A, RNase H, RNase T1, and Mung Bean nuclease.
37. The method of claim 36 wherein said RNase enzyme is Ribonuclease III.
38. The method of claim 34 wherein said fragments have an average size of between about 20 to 500 nucleotides.
39. The method of claim 38 wherein said fragments have an average size of between about 25 to 200 nucleotides.
40. The method of claim 39 wherein said fragments have an average size of between about 50 to 100 nucleotides.
41. The method of claim 34 wherein said detectable label is biotin.
42. The method according to claim 34 wherein said step of end labeling is performed with T4 RNA ligase.